

Remarks

Claims 1-30 are pending in the instant application. Claims 31-58 have been canceled as being drawn to a non-elected invention. Claim 1 has been amended. Support for the claim amendments can be found throughout the application. Therefore, no new matter has been added.

Importantly, the claim cancelations and amendment should not be construed to be an acquiescence to any of the claim rejections. Rather, the cancelations of and amendment to the claims are being made solely to expedite the prosecution of the above-identified application. The Applicants expressly reserve the right to further prosecute the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

Election/Restriction

Examiner acknowledges Applicant's election of the Group I invention and withdraws claims 31-58. Consequently, the Applicants have canceled claims 31-58 without prejudice because they are drawn to non-elected inventions. The Applicants expressly reserve the right to prosecute the canceled claims in one or more divisional applications claiming the benefit of priority to the instant application and its predecessor(s). 35 USC § 121.

Claim Rejections Based on 35 USC § 112¶2

Claims 1-30 stand rejected under 35 USC § 112¶2, based on the Examiner's contention that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner contends that claim 1 is "unclear as to the relationship of a 'a reaction vessel' to the other elements of the apparatus," and the Examiner recommends inserting the phrase "to the reaction vessel" following the word "solvent." In addition, the Examiner contends that claim 22 is unclear "as to the structural relationship of the 'at least one blocking vessel' to the other elements of the apparatus."

In order to expedite prosecution, the Applicants have amended claim 1 as suggested by the Examiner to include the phrase “to the reaction vessel.” Support for this amendment can be found throughout the specification which describes an apparatus having a solution transfer system for transferring the various solutions to the reaction vessel.

Regarding the Examiner’s contention that claim 22 is unclear “as to the structural relationship of the ‘at least one blocking vessel’ to the other elements of the apparatus,” the Applicants point out that this claim simply further requires that the apparatus has a vessel containing a blocking-reagent solution. The blocking vessel holds the blocking agent which can be transferred to the reaction vessel at the appropriate time when it is desirable to install a protecting group on the saccharide substrate. The Applicants contend that the limitation of claim 22 requiring that the apparatus further comprises “at least one blocking vessel containing a blocking reagent solution” particularly points out and distinctly claims the subject matter of the invention. Importantly, the exact structural relationship between the blocking vessel and the other elements of the apparatus recited in claim 1 is not critical. The invention is not limited by the position of the blocking vessel relative to other elements of the apparatus. For example, the location of the blocking vessel relative to the donor vessel is immaterial. Therefore, the Applicants respectfully contend that claim 22 satisfies the requirements of 35 USC § 112¶2.

Accordingly, the Applicants respectfully request the withdrawal of the rejection of claims 1 and 22 under 35 USC § 112¶2.

Rejections Under 35 USC 102/103(a)

Claims 1, 17, and 19 were rejected under 35 USC §102(b) as anticipated by, or under 35 USC §103(a) as obvious, based on Hudson et al. (EP 0 355 266). The Applicants respectfully disagree.

Rebuttal of 35 USC §102(b) Rejections

The Examiner contends that the apparatus in Hudson meets each of the limitations of claim 1. Regarding the limitation in claim 1 that the apparatus contain “at least one

donor vessel containing a saccharide donor solution,” the Examiner states “at least one of the reservoirs R1, R2, R3, R4, R5 and R6 [in the apparatus disclosed in Hudson] inherently comprise ‘a donor vessel’ containing a donor solution, as evidenced by the provision of a solution of ‘Fmoc amino acid’ (Column 9, lines 11-29).” The Examiner further states that “Hudson et al. is silent as to whether the contents of the donor vessel may instead comprise a saccharide donor solution.”

The Applicants contend that Hudson does not form the basis of a proper 35 USC § 102(b) rejection because Hudson, as the Examiner has stated, does not disclose the limitation of claim 1 that the donor vessel contains a saccharide donor solution. The Applicants respectfully remind the Examiner that “a claim is anticipated only if each and every element as set forth in the claim, either expressed in inherently described, is found in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631. Furthermore, the Applicants assert that the mere allusion to using the apparatus to prepare oligosaccharide assemblies as cited by the Examiner in column 1, lines 3-20 of Hudson does not form the basis of a proper 35 USC § 102(b) rejection because the aforementioned statement does not comply with the requirements (e.g., the enablement requirement) of 35 U.S.C. 112¶1. The Applicants point out that Hudson provided no working examples using a saccharide donor solution to prepare an oligosaccharide. Furthermore, the fact that the teachings of Hudson may work to some degree with amino acid substrates does not establish that they may be extended to carbohydrate substrates without the need for undue experimentation. In fact, Hudson does not even provide a working example for synthesizing peptides. Finally, claims 17 and 19 are dependent on claim 1, and hence claims 17 and 19 contain the limitation that the apparatus comprises at least one donor vessel containing a saccharide donor solution.

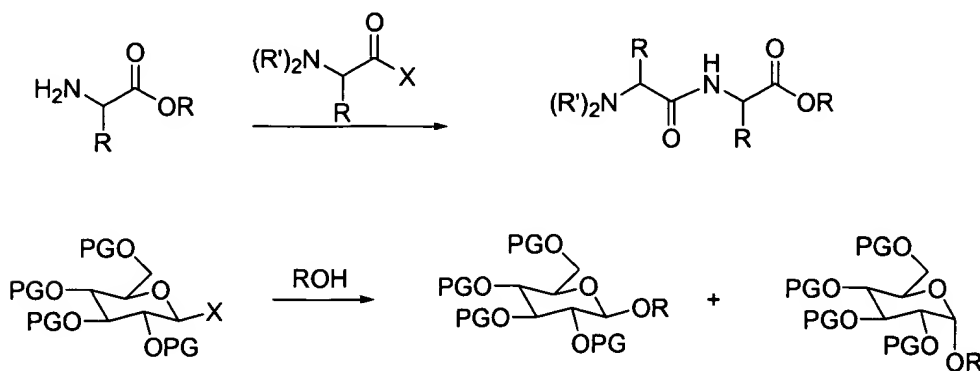
In sum, the Applicants respectfully contend that Hudson does not form the basis of proper 35 USC § 102(b) rejection of claims 1, 17, and 19 because Hudson does not disclose the limitation that the donor vessel contains a saccharide donor solution.

Accordingly, the Applicants respectfully request the withdrawal of the rejection of claims 1, 17, and 19 under 35 USC § 102(b).

Rebuttal of 35 USC § 103(a) Rejections

The Examiner contends that it would have been obvious, absent any unexpected results, for one of ordinary skill in the art to use a saccharide donor solution in the apparatus of Hudson based on its alleged suitability for the intended use of synthesizing oligosaccharides. In response, the Applicants contend that Hudson does not form the basis of a proper rejection under 35 USC § 103(a) because one of ordinary skill in the art would not have a reasonable expectation of success in automated solid-phase synthesis of oligosaccharides based on the teachings of Hudson. The Applicants respectfully remind the Examiner that a *prima facie* case of obviousness requires a reasonable expectation of success. *MPEP 2143.02*. The Applicants contend one of ordinary skill in the art would not have a reasonable expectation of success in using the apparatus described in Hudson for automated solid-phase synthesis of oligosaccharides because the synthesis of oligosaccharides is much more difficult than the synthesis of peptides. One reason that oligosaccharides are more difficult to synthesize is that the reaction forming the bond between the two saccharides can generate two stereoisomers; this fact stands in contrast to peptide coupling in which there is no possibility for the formation of stereoisomers because an amide moiety is planar. See Scheme 1 below.

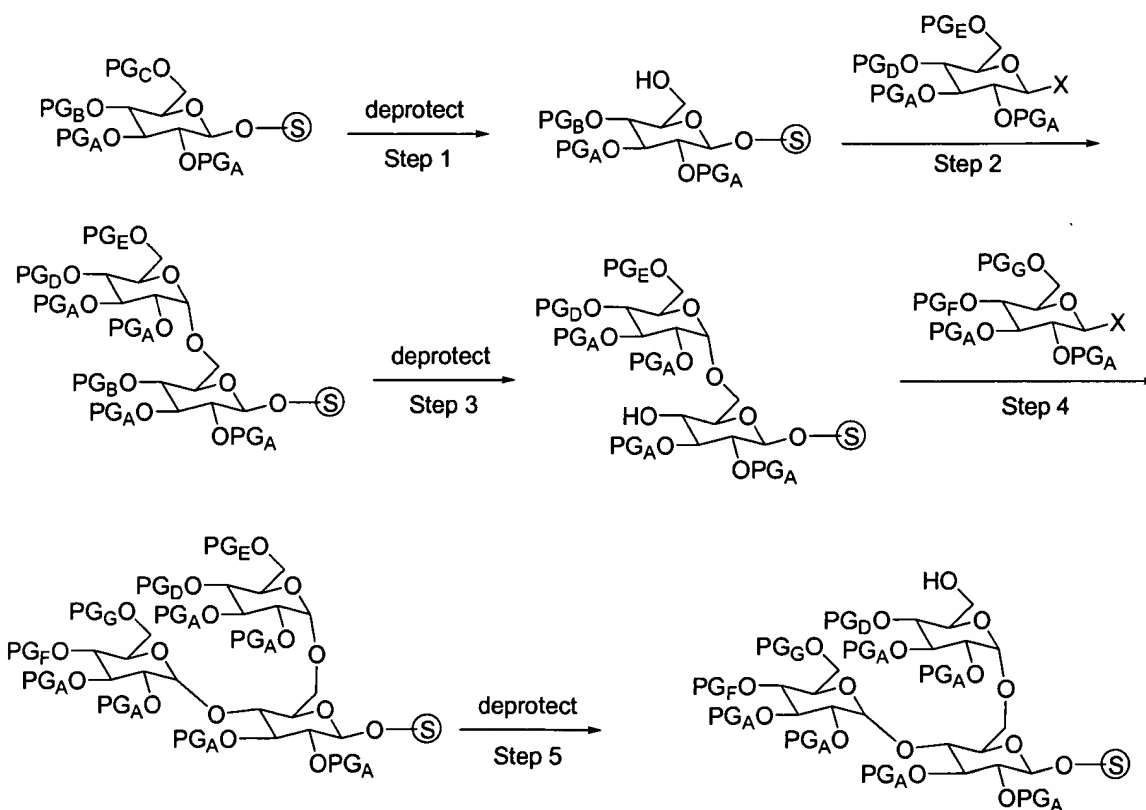
Scheme 1.



Another reason that oligosaccharides are more difficult to synthesize than oligopeptides is because many oligosaccharides contain branching structures. In contrast, peptides are linear structures and extension of the amino acid sequence requires only one

deprotection step after each amino acid is added. The synthesis of branched oligosaccharides requires multiple deprotection steps in order to extend rationally the oligosaccharide sequence. Furthermore, the deprotection steps must be carefully controlled to prevent inadvertent deprotection of other protecting groups on the oligosaccharide. The synthesis of a branched oligosaccharide is represented in Scheme 2 below.

Scheme 2.



Scheme 2 illustrates that synthesis of a branched saccharide sequence requires a first deprotection in step 1, stereoselective coupling of a first saccharide in step 2, a second selective deprotection in step 3, a second stereoselective coupling in step 4, and a third selective deprotection in step 5. Importantly, each of the protecting groups must be amenable to selective installation and removal. Inadvertent removal of protecting groups leads to side products, thereby decreasing the yield and purity of the final product. Furthermore, synthesis of a second branching point requires even more deprotection and

coupling steps in order to extend the length of the oligosaccharide backbone by a single saccharide unit. In contrast, peptide synthesis does not require the careful manipulation of multiple protecting groups or multiple deprotection steps to the same extent required for oligosaccharide synthesis because peptides are linear structures.

The fact that oligosaccharide synthesis is very difficult has been acknowledged by leading experts in oligosaccharide synthesis. Professor Chi-Huey Wong of Scripps Research Institute states that oligosaccharides are more difficult to synthesize than peptides. *See* Sears, P.; Wong, C.-H. *Science* **2001**, *291*, 2344, page 2344, first paragraph; a copy of which is provided herewith as **Exhibit A**. Professor Wong states that oligosaccharide synthesis is difficult because the “monosaccharide units can be connected by α or β linkages,” and oligosaccharide synthesis “requires multiple selective protection and deprotection steps.” *See id.* Importantly, Hudson provides no direction for oligosaccharide synthesis, and hence no direction as to how to overcome the above-mentioned obstacles in oligosaccharide synthesis. The Applicants respectfully remind the Examiner that “evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness.” *See MPEP 2143.02; MPEP 2143; and In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). Therefore, the Applicants contend that one of ordinary skill in the art would have no reasonable expectation of success in automated synthesis of oligosaccharides on solid-phase based solely on the teachings of Hudson.

Accordingly, the Applicants respectfully request the withdrawal of the rejection of claims 1, 17, and 19 under 35 USC § 103(a).

Rejections Under 35 USC § 103(a)

Various sets of claims stand rejected under 35 USC § 103(a), based on the Examiner’s contentions that they are made obvious by various patents or publications or combinations thereof. To better organize the Applicants’ traverses of the Examiner’s rejections under 35 USC 103(a), they are set forth below in paragraphs numbered corresponding to the numbering scheme used in the Office Action.

6. Claims 2-5, 8-14, 18, 20, 21, 26-28, and 30 were rejected under 35 USC § 103(a) based on the Examiner's contention that they are obvious based on Hudson et al. (EP 0 355 266) in view of U.S. Patent 6,323,339 ("the '339 patent"). The Applicants contend that Hudson et al. in view of the '339 patent does not form the basis of a proper 35 USC §103(a) rejection of claims 2-5, 8-14, 18, 20, 21, 26-28, and 30 because the '339 patent is not available as prior art under 35 USC §103(a).

The '339 patent is not available as prior art under 35 USC § 103(a) because the '339 patent does not qualify as prior art under 35 USC § 102(a), 102(b), or 102(e). The Applicants remind the Examiner that the present application was filed on August 17, 2001; and claims priority to U.S. Provisional Application 60/254,233, filed on December 8, 2000 and U.S. Provisional Application 60/226,169, filed on August 18, 2000. The '339 patent issued on November 27, 2001 which is after the filing date of the instant application, hence the '339 patent is not prior art under 35 USC § 102(a) or 102(b). Regarding 35 USC § 102(e), the inventors listed on the '339 patent, Peter H. Seeberger and Obadiah J. Plante, are the same inventors of the instant application. Therefore, the '339 patent is not prior art under 35 USC § 102(e) because the '339 patent is not "by another."

Furthermore, the Applicants contend that one of ordinary skill in the art would have no reasonable expectation of success in automated synthesis of oligosaccharides on solid-phase based solely on Hudson for the reasons stated above with regard to claim 1. The Applicants respectfully remind the Examiner that claims 2-5, 8-14, 18, 20, 21, 26-28, and 30 are dependent on claim 1 which the Applicants contend is not obvious based on Hudson, and *MPEP* 2143.03 states that "if an independent claim is nonobvious under 35 USC § 103, then any claim depending therefrom is nonobvious." *In re Fine*, 837 F.2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988).

Accordingly, the Applicants respectfully request the withdrawal of the rejection of claims 2-5, 8-14, 18, 20, 21, 26-28, and 30 under 35 USC § 103(a).

7. Claims 6 and 7 were rejected under 35 USC § 103(a) based on the Examiner's contention that they are obvious based on Hudson et al. (EP 0 355 266) in view of U.S. Patent 6,323,339 ("the '339 patent"), and further in view of U.S. Patent 4,610,847 ("the '847 patent"). The Applicants respectfully disagree.

First, the Applicants remind the Examiner that the '339 patent is not available as prior art under 35 USC § 103(a) because it does not qualify as prior art under 35 USC § 102(a), 102(b), or 102(e) as described above. Second, the Applicants contend that Hudson et al. in view of the '847 patent does not form the basis of a proper 35 USC § 103(a) rejection of claims 6 and 7 because one of ordinary skill in the art would have no reasonable expectation of success in automated synthesis of oligosaccharides on solid-phase for the reasons stated above with regard to claim 1.

Furthermore, the '847 patent relates to a conversion flask and provides no additional guidance for oligosaccharide synthesis. The Applicants respectfully remind the Examiner that claims 6 and 7 are dependent on claim 3 which in turn is dependent on claim 1. The Applicants respectfully contend that they have effectively rebutted the Examiner's rejection of 1 under 35 USC § 103(a). Finally, *MPEP* 2143.03 states that "if an independent claim is nonobvious under 35 USC § 103, then any claim depending therefrom is nonobvious." *In re Fine*, 837 F.2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988).

Accordingly, the Applicants respectfully request the withdrawal of the rejection of claims 6 and 7 under 35 USC § 103(a).

8. Claims 15 and 29 were rejected under 35 USC § 103(a) based on the Examiner's contention that they are obvious based on Hudson et al. (EP 0 355 266) in view of Seeberger et al. *Organic Letters* **1999**, *1*, 1811. The Applicants respectfully disagree.

The Applicants contend that Hudson et al. in view of Seeberger et al. does not form the basis of a proper 35 USC § 103(a) rejection of claims 15 and 29 because Seeberger et al. is not available as prior art under 35 USC § 103(a). The Seeberger article is not available as prior art under 35 USC § 103(a) because the article does not qualify as prior art under 35 USC § 102(a) or 102(b). The Applicants remind the Examiner that the

present application was filed on August 17, 2001; and claims priority to U.S. Provisional Application 60/254,233, filed on December 8, 2000 and U.S. Provisional Application 60/226,169, filed on August 18, 2000. The *Organic Letters* article by Seeberger et al. was published on the Internet on October 28, 1999. Therefore, the Seeberger article is not prior art under 35 USC § 102(b) because it was not published more than 1 year prior to the earliest effective filing date (August 18, 2000) of the instant application.

With respect to 35 USC §102(a), the Applicants contend that the article presented in *Organic Letters* 1999, 1, 1811 does not qualify as prior art under 35 USC § 102(a) because the journal article describes the Applicants' work. See *MPEP* 715.01(c) and 2132.01. The Applicants assert that the subject matter described in the *Organic Letters* article was invented by Peter H. Seeberger and Obadiah J. Plante, the co-inventors of the instant application. Co-authors Rodrigo B. Andrade and Luis G. Melean on the article presented in *Organic Letters* 1999, 1, 1811 merely carried out assignments and worked under the supervision and direction of Peter H. Seeberger. Accordingly, pursuant to 37 CFR 1.132, the Applicants submit herewith unexecuted copies of declarations by Peter H. Seeberger and Obadiah J. Plante as evidence that the article presented in *Organic Letters* 1999, 1, 1811 describes the Applicants' work; i.e., that neither Andrade nor Melean is an inventor of anything disclosed in the publication. The Applicants respectfully remind the Examiner that "an affidavit or declaration by Applicant alone indicating that the Applicant is the sole inventor and that the others [listed as co-authors on the publication] were merely working under his or her direction is sufficient to remove the publication as a reference under 35 USC §102(a)." See *In re Katz*, 687 F.2d 450 and *MPEP* 715.01(c). The Applicants will promptly submit executed copies of the aforementioned declarations to the USPTO upon receipt from the inventors.

In light of the showing that the *Organic Letters* article is not available as prior art under 35 USC § 103(a), the Applicants contend that rejection of claims 15 and 29 under 35 USC §103(a) based on Hudson et al. would not be proper because Hudson alone does not teach all the limitations of claims 15 and 29. As stated by the Examiner, Hudson is "silent as to the deblocking reagent comprising sodium methoxide," and Hudson is "silent

as to the at least one insoluble resin bead comprising an octenediol functionalized resin.” Hence, Hudson does not teach the limitation of claim 15 that the at least one deblocking vessel contains a solution comprising sodium methoxide. Furthermore, Hudson does not teach the limitation of claim 29 that the at least one insoluble resin bead is comprised of an octenediol functionalized resin. The Applicants respectfully remind the Examiner that in order “to establish a *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.” *MPEP* 2143.03. *See also In re Royka*, 490 F.2d 981.

Finally, the Applicants contend that one of ordinary skill in the art would have no reasonable expectation of success in a automated synthesis of oligosaccharides on solid-phase based solely on Hudson for the reasons stated above with regard to claim 1. The Applicants respectfully remind the Examiner that claims 15 and 29 are both dependent on claim 1 which the Applicants contend is not obvious based on Hudson; *MPEP* 2143.03 states that “if an independent claim is nonobvious under 35 USC § 103, then any claim depending therefrom is nonobvious.” *In re Fine*, 837 F.2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988).

Accordingly, the Applicants respectfully request the withdrawal of the rejection of claims 15 and 29 under 35 USC § 103(a).

9. Claim 16 was rejected under 35 USC §103(a) based on the Examiner’s contention that it is obvious based on Hudson et al. (EP 0 355 266) in view of U.S. Patent 5,403,927 (“the ‘927 patent”) to Bendiak. Specifically, the Examiner states that “Hudson et al. is silent as to the blocking solution comprising hydrazine,” but “Bendiak evidences the use of hydrazine as a deblocking reagent.” The Applicants contend that Hudson et al. in view of the ‘927 patent do not form the basis of a proper 35 USC §103(a) rejection of claim 16 because there is no suggestion or motivation to combine the ‘927 patent with Hudson.

As stated by the Examiner, the ‘927 patent teaches the use of hydrazine for “the sequential removal of monosaccharides from the reducing end of oligosaccharides, by teaching the, ‘cleaving [of] the glycosidic bond between the former reducing end

monosaccharide and the adjacent monosaccharide of the oligosaccharide using a hydrazine.” Hence, the ‘927 patent teaches the destruction of oligosaccharides. In contrast, the present application relates to *synthesizing* oligosaccharides, not *degrading* oligosaccharides. Therefore, one of ordinary skill in the art would have no motivation to combine the ‘927 patent with Hudson for the purpose of synthesizing oligosaccharides.

The Examiner is reminded that “the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.” *MPEP* 2143.01 and *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Accordingly, the Applicants respectfully request the withdrawal of the rejection of claim 16 under 35 USC § 103(a) based on Hudson in view of the ‘927 patent.

10. Claims 22-25 were rejected under 35 USC §103(a) based on the Examiner’s contention that they are obvious based on Hudson et al. (EP 0 355 266) in view of U.S. Patent 5,256,549 (“the ‘549 patent”). In response, the Applicants contend that Hudson et al. in view of the ‘549 patent does not form the basis of a proper 35 USC §103(a) rejection of claims 22-25 because one of ordinary skill in the art would have no reasonable expectation of success in an automated synthesis of oligosaccharides on solid-phase for the reasons described with regards to claim 1 above. The arguments presented regarding claim 1 above apply directly to claims 22-25 because the ‘549 patent provides no additional guidance for oligosaccharide synthesis. Furthermore, neither Hudson nor the ‘549 patent specifically teach using benzyl trichloroacetimidate. Therefore, Hudson in view ‘549 patent does not form the basis of a proper 35 USC §103(a) rejection of claim 23 because neither Hudson nor ‘549 patent teach the limitation that the blocking vessel contains benzyl trichloroacetimidate. The Applicants respectfully remind the Examiner that in order “to establish a *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.” See *MPEP* 2143.03 and *In re Royka*, 490 F.2d 981.

Accordingly, the Applicants respectfully request the withdrawal of the rejection of claims 22-25 under 35 USC § 103(a) based on Hudson in view of the ‘549 patent.


Fees

The Applicants believe they have provided for the required fees in connection with the filing of this paper. Nevertheless, the Director is hereby authorized to charge any additional required fee to our Deposit Account, 06-1448.

Conclusion

In view of the above amendments and remarks, it is believed that the pending claims are in condition for allowance. Therefore, the Applicants respectfully request reconsideration and withdrawal of the pending rejections. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to contact the undersigned.

Respectfully submitted,
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